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Chapter 22: Constipation

INTRODUCTION

- *Definition: Constipation* is the difficult or infrequent passage of stool, at times associated with straining or a feeling of incomplete defecation. The condition is considered chronic if symptoms last for at least 3 months.
- Constipation may be primary (occurs without an underlying identifiable cause) or secondary (the result of constipating drugs, lifestyle factors, or medical disorders).
- Constipation commonly results from a diet low in fiber, inadequate fluid intake, decreased physical activity, or from use of constipating drugs such as opioids.
- Causes of drug-induced constipation are listed in **Table 22-1**. All opioid derivatives are associated with constipation, but the degree of intestinal inhibitory effects seems to differ among agents. Orally administered opioids appear to have a greater inhibitory effect than parenterally administered agents.

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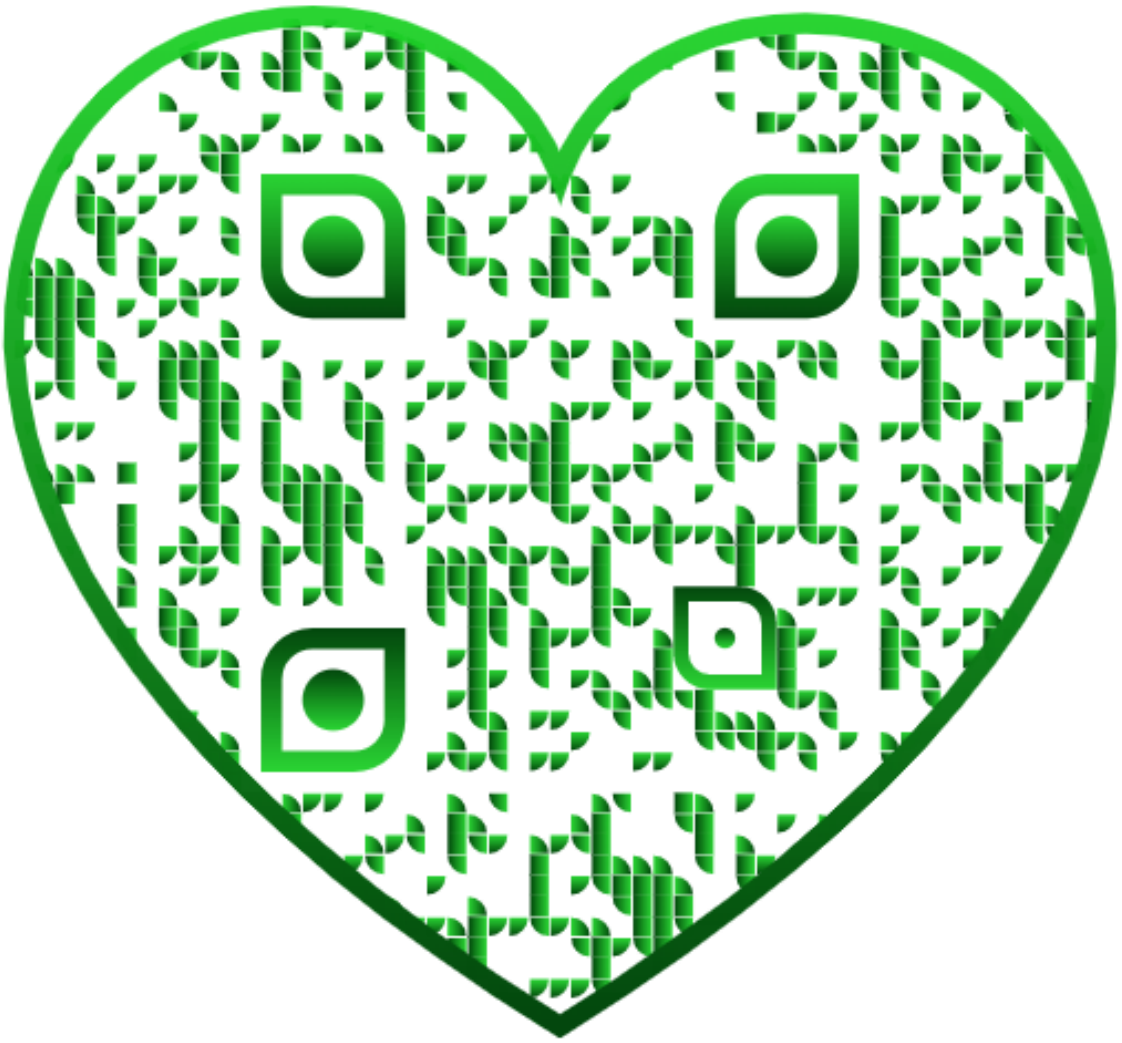

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TABLE 22-1

Drugs Causing Constipation

Analgesics Inhibitors of prostaglandin synthesis Opioids Nonsteroidal anti-inflammatory agents
Anticholinergics Antihistamines Antiparkinsonian agents (eg, benztropine or trihexyphenidyl) Phenothiazines Tricyclic antidepressants
Antacids containing calcium carbonate or aluminum hydroxide
Barium sulfate
Calcium channel antagonists
Clonidine
Diuretics (non–potassium-sparing)
Ganglionic blockers
Iron preparations
Muscle blockers (D-tubocurarine, succinylcholine)
Polystyrene sodium sulfonate

CLINICAL PRESENTATION

- The general clinical presentation of constipation is listed below. According to the Rome IV criteria, patients should have at least two of the signs and symptoms listed below which apply to a minimum of 25% of bowel movements.
- A complete and thorough history should be obtained from the patient, including the frequency of bowel movements and duration of symptoms. The patient should also be carefully questioned about usual diet and laxative regimens.
- General health status, signs of underlying medical illness (ie, hypothyroidism), and psychological status (eg, depression or other psychological illness) should be assessed.
- Patients with “alarm symptoms,” a family history of colon cancer, or those older than 50 years with new symptoms may need further diagnostic evaluation.
- **Signs and symptoms**:

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✓ Infrequent bowel movements (<3 per week).

✓ Stools that are hard, small, or dry.

✓ Straining.

✓ Feeling of incomplete evacuation.

✓ Feeling of anorectal obstruction or blockage.

✓ Physical tactics needed for defecation.

✓ Loose stools rarely occur without laxative use.

- **Alarm signs and symptoms**:

✓ Hematochezia.

✓ Melena.

✓ Family history of colon cancer.

✓ Family history of inflammatory bowel disease.

✓ Anemia.

✓ Unintentional weight loss of >10% of body weight.

✓ Anorexia.

✓ Nausea and vomiting.

✓ Severe, persistent constipation that is refractory to treatment.

✓ New-onset or worsening constipation in elderly without evidence of primary cause.

- **Physical examination**:

✓ Perform rectal exam to check for the presence of anatomical abnormalities (such as fistulas, fissures, hemorrhoids, rectal prolapse) or abnormalities of perianal descent.

✓ Digital examination of rectum to check for fecal impaction, anal stricture, or rectal mass.

- **Laboratory and other diagnostic tests**:

✓ No routine recommendations for lab testing—as indicated by clinical discretion.

✓ In patients with signs and symptoms suggestive of organic disorder, specific testing may be performed (ie, thyroid function tests, electrolytes, glucose, complete blood count) based on clinical presentation.

✓ In patients with alarm signs and symptoms or when structural disease is a possibility, select appropriate diagnostic studies: rectal balloon expulsion test (BET), anorectal manometry, colonoscopy, barium enema.

TREATMENT

- Goals of Treatment: The major goals of treatment are to: (a) relieve symptoms; (b) reestablish normal bowel habits; and (c) improve quality of life by minimizing adverse effects of treatment.

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GENERAL APPROACH

- If an underlying disease is recognized as the cause of constipation, attempts should be made to correct it. GI malignancies may be removed through a surgical resection. Endocrine and metabolic derangements are corrected by the appropriate methods.
- If a patient is consuming medications known to cause constipation, consideration should be given to alternative agents. If no reasonable alternatives exist to the medication thought to be responsible for constipation, consideration should be given to lowering the dose. If a patient must remain on constipating medications, more attention must be given to general measures for prevention of constipation.
- The proper management of constipation requires a combination of nonpharmacologic and pharmacologic therapies.

NONPHARMACOLOGIC THERAPY

- The most important aspect of the therapy for constipation is dietary modification to increase the amount of fiber consumed. Gradually increase daily fiber intake to 20–30 g, either through dietary changes or through fiber supplements. Fruits, vegetables, and cereals have the highest fiber content.
- A trial of dietary modification with high-fiber content should be continued for at least 1 month. Most patients begin to notice effects on bowel function 3–5 days after beginning a high-fiber diet.
- Patients with constipation due to pelvic floor dysfunction/disordered defecation may have a less favorable response to fiber therapy than other constipation subtypes. Many adult patients with functional defecatory disorders appear to benefit from pelvic floor retraining with biofeedback therapy.
- Abdominal distention and flatus may be particularly troublesome in the first few weeks, particularly with high bran consumption.

PHARMACOLOGIC THERAPY

- The laxatives are divided into three classifications: (1) those causing softening of feces in 1–3 days, (2) those resulting in soft or semifluid stool in 6–12 hours, and (3) those causing water evacuation in 1–6 hours.
- Other agents include intestinal secretagogues, opioid antagonists, and a prokinetic agent.
- Dosage recommendations for laxatives and cathartics are provided in **Table 22-2**.

TABLE 22-2

Dosage Recommendations for Pharmacologic Therapy

Agent	Recommended Adult Dose
Agents that Cause Softening of Feces in 1–3 Days	
Bulk-forming agents	
Methylcellulose	Varies with product
Polycarbophil	4–6 g/day
Psyllium	Varies with product
Emollients	
Docusate sodium	50–360 mg/day

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Docusate calcium	50–360 mg/day
Docusate potassium	100–300 mg/day
Osmotic laxatives	
Polyethylene glycol 3350	17 g/dose
Lactulose	15–30 mL orally
Lactitol	20 g/day orally
Sorbitol	30–50 g/day orally
Agents that Result in Soft or Semifluid Stool in 6–12 Hours	
Bisacodyl (oral)	5–15 mg orally
Senna	Dose varies with formulation
Magnesium sulfate (low dose)	<10 g orally
Agents that Cause Watery Evacuation in 1–6 Hours	
Magnesium citrate	18 g in 300 mL water
Magnesium hydroxide	2.4–4.8 g orally
Magnesium sulfate (high dose)	10–30 g orally
Sodium phosphates	Varies with salt used
Bisacodyl	10 mg rectally
Polyethylene glycol–electrolyte preparations	4 L for bowel cleansing
Intestinal Secretagogues	
Lubiprostone	24 mcg orally twice daily
Linaclotide	145 mcg orally daily
Plecanatide	3 mg orally daily
Opioid Antagonists	
Methylnaltrexone	450 mg orally daily or 12 mg subcutaneously daily
Naloxegol	25 mg daily
Naldemedine	0.2 mg daily

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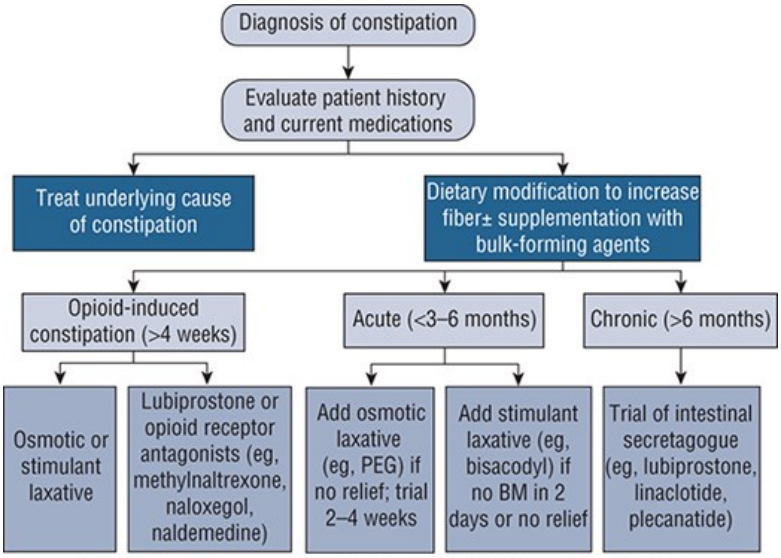
Prokinetics	
Prucalopride	2 mg daily

Recommendations

- A constipation treatment algorithm is presented in **Fig. 22-1**.
- Osmotic laxative therapy is considered the preferred first line for the treatment of constipation, in addition to increasing dietary fiber or using fiber supplementation.
- Patients are often encouraged to increase daily fluid intake and physical activity as well as dedicate time to respond to the urge to defecate, although efficacy data are conflicting for these measures.

FIGURE 22-1

A general treatment algorithm for constipation.


Diagnosis of constipation
Evaluate patient history and current medications
Treat underlying cause of constipation
Dietary modification to increase fiber± supplementation with bulk-forming agents
Opioid-induced constipation (>4 weeks)
Acute (<3–6 months)
Chronic (>6 months)
Osmotic or stimulant laxative
Lubiprostone or opioid receptor antagonists (eg, methylnaltrexone, naloxegol, naldemedine)
Add osmotic laxative (eg, PEG) if no relief; trial 2–4 weeks
Add stimulant laxative (eg, bisacodyl) if no BM in 2 days or no relief
Trial of intestinal secretagogue (eg, lubiprostone, linaclotide, plecanatide)

Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Lisa M. Holle, Cecily V. DiPiro: *DiPiro's Pharmacotherapy Handbook, 13th Edition*
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Emollient Laxatives (Docusates)

- **Docusates** are surfactant agents that increase water and electrolyte secretion in the small and large bowel and result in a softening of stools within 1–3 days.
- Emollient laxatives are not effective in treating constipation but are used mainly to prevent constipation. They may be helpful in situations where straining at stool should be avoided, such as after recovery from myocardial infarction, with acute perianal disease, or after rectal surgery.
- It is unlikely that these agents are effective in preventing constipation if major causative factors (eg, heavy opiate use, uncorrected pathology, and inadequate dietary fiber) are not concurrently addressed.

Lactulose

- **Lactulose** is generally not recommended as a first-line agent for the treatment of constipation because it is costly and may cause flatulence,

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nausea, and abdominal discomfort or bloating. It may be justified as an alternative for acute constipation or in patients with an inadequate response to increased dietary fiber and bulking agents.

Magnesium Salts

- Magnesium salts, including hydroxide, phosphate, and citrate, and sodium phosphate are categorized as saline cathartics. These agents are frequently used as bowel preparations prior to diagnostic procedures such as colonoscopy.
- Milk of magnesia (an 8% suspension of magnesium hydroxide) may be used occasionally to treat constipation in otherwise healthy adults, but efficacy data are limited.
- Saline cathartics should not be used on a routine basis. These agents may cause fluid and electrolyte depletion. Also, magnesium or sodium accumulation may occur in patients with renal dysfunction or congestive heart failure. These risks increase with long-term use.

Glycerin

- **Glycerin** is usually administered as a suppository and with an onset of action usually less than 30 minutes. Glycerin is considered a safe laxative, although it may occasionally cause rectal irritation. Its use is acceptable on an intermittent basis for constipation, particularly in children.

PEG–Electrolyte Lavage Solution

- Low doses of PEG solution (10–30 g or 17–34 g per 120–240 mL) once or twice daily may be used for treatment of constipation. Daily use in low dose (17 g) may be safe and effective for up to 6 months.
- The most common adverse effects are GI-related and include nausea, vomiting, flatulence, and abdominal cramping.

Stimulant Laxatives

- Stimulant laxatives such as diphenylmethane (bisacodyl) and anthraquinone (senna and others) derivates are expected to cause a bowel movement within 8–12 hours of administration.
- They are typically reserved for intermittent use or in patients who fail to respond adequately to bulking and osmotic laxatives. Some patients with severe chronic constipation and nonmodifiable risk factors may use these agents on a more regular basis.

Lubiprostone and Linaclotide

- **Lubiprostone** (Amitiza) is approved for chronic idiopathic constipation as well as for opioid-induced constipation (OIC). The dose is one 24-mg capsule twice daily with food. Lubiprostone may cause nausea, headache, and diarrhea.
- Lubiprostone is reserved for patients with chronic constipation who fail conventional first-line agents such as osmotic laxatives and fiber supplementation, or for those with OIC.
- **Linaclotide** (Linzess) is approved for the treatment of constipation and IBS with constipation (IBS-C). Seventy-two-mcg and 145-mcg doses can be taken on an empty stomach at least 30 minutes before the first meal of the day. It should not be used in patients younger than 18 years of age.
- **Plecanatide** is approved for chronic idiopathic constipation in an adult dose of 3 mg given once daily without regard to food. It is contraindicated in children < 6 years of age and should be avoided in those 6–18 years.

Opioid-Receptor Antagonists and Prucalopride

- Alvimopan is an oral GI-specific μ-receptor antagonist for short-term use in hospitalized patients to accelerate recovery of bowel function after large or small bowel resection. It is given as one 12-mg (capsule) 30 minutes–5 hours before surgery and then 12 mg twice daily for up to 7 days or until hospital discharge (maximum 15 doses). It is contraindicated in patients receiving therapeutic doses of opioids for more than 7 consecutive days prior to surgery.

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- Methylnaltrexone is another μ-receptor antagonist approved for OIC in patients with advanced disease receiving palliative care or when response to laxative therapy has been insufficient for OIC with chronic noncancer pain.
- Other opioid-receptor antagonists include naloxegol and naldemedine.
- Prucalopride is a selective 5-hydroxytryptamine-4 (5-HT4) receptor agonist used for chronic constipation.

See Chapter 57, Diarrhea, Constipation, and Irritable Bowel Syndrome, authored by Patricia H. Fabel and Kayce M. Shealy, for a more detailed discussion of this topic.

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